REMARKS

Status of the Claims

Claims 1, 22, and 23 are pending in the present application. Claims 2-21 were previously canceled. Claims 24-28 are presently canceled. Claims 22 and 23 are withdrawn from consideration as directed to a non-elected invention. Claim 1 is amended for clarity according to the Examiner's suggestions. Claim 1 is further amended to cancel the drugs previously specified in the claim except for methamphetamine. Claims 22 and 23 are amended for consistency with independent, amended, claim 1.

No new matter has been added by way of this amendment. Reconsideration is respectfully requested.

Statement of Substance of the Interview

Applicants and Applicants' representative thank the Examiner for extending the courtesy of an interview on June 10, 2010. During the interview, the further restriction requirement was discussed. The Examiner stated that the withdrawal of claims 22, 23, 25, 26, and 28 was due to the scope of previously pending claim 1. In particular, the Examiner noted that previously pending claim 1 does not require the elected polymorphism, but is only one of many polymorphisms that may be used in the claimed method. The Examiner further stated that the withdrawn claims would be rejoined if claim 1 were amended to require the elected polymorphism.

The rejection under 35 U.S.C. § 112, first paragraph, enablement was also discussed during the interview. The Examiner suggested evidence that could be provided to further support enablement of the claimed subject matter.

Request for Rejoinder

As noted above, the Examiner indicated during the June 10, 2010, interview that the claims withdrawn in the March 19, 2010, Office Action could be rejoined with claim 1, provided that claim 1 were amended to require the elected polymorphism. Claim 1 is amended accordingly. In view of the amendment, Applicants request rejoinder of pending, withdrawn claims 22 and 23.

Objections to the Amendments to the Specification

The Examiner states that the amendments to the specification submitted on November 16, 2009, introduce new matter into the disclosure, *see* Office Action, pages 3-4, item 3. This objection is respectfully traversed.

Specifically, the Examiner states that newly presented SEQ ID NO: 100, which is referenced in the amendment to Table 4, is not supported by the present application. The Examiner further states that amended Table 6, which describes a new linkage disequilibrium value for the IVS +6151 and +8449 positions, is also not supported in the originally filed application.

Table 4 and SEQ ID NO: 100

Applicants submit that the instant application adequately supports SEQ ID NO: 100 and amended Table 4. Applicants reiterate that the instant application specifically teaches that oligonucleotides having 101 bases with a described polymorphism at the 51st base are contemplated, *see*, for example, page 25 of the originally filed application and previously pending Table 4. Accordingly, a 101 base sequence, wherein base 51 is the mutation TAA + G2025A, is encompassed by the originally filed application. Further, as noted in the November 16, 2009, response, an ordinary artisan recognizes from the term "TAA + G2025A", where the polymorphism is located within the mu-opioid receptor gene. Therefore, an ordinary artisan would have been able to envision the TAA + G2025A polymorphism, the location of the polymorphism, and the nucleotides surrounding this polymorphism. Accordingly, Applicants submit that an ordinary artisan could have envisioned the 101 base oligonucleotide sequence described in SEQ ID NO: 100 and the polymorphism at base 51, from the information disclosed in the present application.

In view of the foregoing, Applicants believe that there is basis in the originally filed application for SEQ ID NO: 100 and the amendment to Table 4. Withdrawal of the objection is respectfully requested.

Table 6

Applicants submit that the instant application adequately supports the linkage disequilibrium value for the IVS +6151 and +8449 positions described in amended Table 6. Applicants reiterate that the significance of the linkage disequilibrium values, as described in amended Table 6, is inherent in the population described in the present application. An ordinary

artisan, repeating the linkage disequilibrium analysis with the population described in the present application would have determined that the reported D' and r^2 values actually reach significance.

In view of the foregoing, Applicants believe that there is basis in the originally filed application for amended Table 6. Withdrawal of the objection is respectfully requested.

Issues under 35 U.S.C. § 112, second paragraph

Claims 1, 24, and 27 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, *see* Office Action, pages 5-6, item 6. Applicants respectfully traverse.

Specifically, the Examiner states that the recitation "IVS3 + A6151G of SEQ ID NO: 28" is unclear and suggests that claim 1 be amended to specify "IVS3 + A6151G of the human mu opioid receptor gene, wherein IVS3 + A6151G is either an A or a G in the position in the mu opioid receptor gene corresponding to position 51 of SEQ ID NO: 28."

Claims 24 and 27 are canceled. Accordingly, the rejection is moot in regard to these claims.

In an effort to expedite prosecution, claim 1 is amended according to the Examiner's suggestions. Further, the additional polymorphisms described in claims 1, 22, and 23, are similarly amended. Accordingly Applicants believe that this aspect of the rejection is overcome.

Claims 1, 24, and 27 are further rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for the recitation "wherein said gene polymorphisms are in linkage disequilibrium with IVS3 + A6151G of SEQ ID NO: 28." The Examiner states that it is unclear how IVS3 + A6151G can be in linkage disequilibrium with itself.

In an effort to expedite prosecution, claim 1 is amended to clarify that "the method, optionally, further comprises linking gene polymorphisms that are in linkage disequilibrium with IVS3 + A6151G, said gene polymorphisms in linkage disequilibrium with IVS3 + A6151G being selected from the group consisting of" the described polymorphisms.

In view of the foregoing, Applicants believe the instant amended claims are not unclear. Accordingly, withdrawal of the rejection is respectfully requested.

Issues under 35 U.S.C. §112, first paragraph

Claims 1, 24, and 27 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, *see* Office Action, pages 6-13, item 7. Applicants respectfully traverse.

According to the Examiner, Table 10 of the instant specification teaches that one study population demonstrates an association between the IVS3 + A6151G polymorphism and methamphetamine sensitivity, however, no such association is observed in a second study population. The Examiner further states that the specification does not support a consistent measure of strong linkage disequilibrium between IVS3+ 6151 and IVS3 + 8449. In view of this assertion, the Examiner does not find the post-filing data or the Declarations submitted on November 16, 2009, and December 1, 2009, to persuasively demonstrate the association between polymorphisms in linkage disequilibrium with IVS3 + 6151 and drug sensitivity. In addition, the Examiner states that the provided post-filing data, which shows an association between IVS3+A6151G and drug sensitivity, only describe an association between "24 hour postoperative" fentanyl, which is not specifically described in the instant application. Overall, the Examiner believes that any asserted associations between the polymorphisms described in the present claims and any type of drug sensitivity, including methamphetamine addiction, are unpredictable, and accordingly, fail to comply with the requirement of 35 U.S.C. § 112, first paragraph.

Claims 24 and 27 are canceled. Accordingly, the rejection is moot in regard to these claims.

Applicants do not agree that the instant application fails to support the subject matter of the pending claims. Nevertheless, in an effort to expedite prosecution, the claims are amended to specify that the described polymorphism is linked "to individual methamphetamine sensitivity."

Applicants submit that the present application adequately supports the amended claims. Table 10 demonstrates a statistically significant association between the elected polymorphism and psychosis occurring within three years from the start of methamphetamine use. Accordingly, Table 10 adequately demonstrates an association between the elected polymorphism and methamphetamine sensitivity.

Table 10 further indicates that there is no statistically significant association between the elected polymorphism and psychosis occurring after three years from the start of methamphetamine use. However, Applicants submit that this symptom is not relevant to methamphetamine sensitivity.

In particular, Applicants note that when methamphetamine addiction is prolonged, any methamphetamine user is likely to develop delusions or hallucinations. Accordingly, an ordinary artisan recognizes that after three years of methamphetamine use, polymorphisms would not have been predictive of the onset of psychosis since psychotic symptoms are likely to occur in all

users after three years. Therefore, an ordinary artisan recognizes that the second study population described in Table 10, (group 2), is not relevant to methamphetamine sensitivity.

In view of the foregoing, the population described in the instant application, which demonstrates an association between early onset of psychosis after methamphetamine use and the elected polymorphism, is not contradicted by results obtained from the second study population. Accordingly, the instant application adequately enables the instant claims. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should there by any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, Ph.D., Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: JUN 21 2010

Respectfully submitted,

By _____

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